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EXAMINER
DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
1642	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

SM

Office Action Summary	Application No.	Applicant(s)	
	09/847,046	HEVEZI ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *1-6 and 8-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7 and 39-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election with traverse of group II, claims 7, 39-43 in Paper No. 10 is acknowledged. The traversal is on the ground(s) that both inventions could be searched without undue burden, and the Examiner must show that the restricted groups have different classification, acquired a separate status in the art, or that searching would require different fields of search. This is not found persuasive because the two groups have different subclasses, the searches for the level of mRNAs and the level of the encoded protein require different searches and are not co-extensive, and it would be undue burden for the Examiner to search the two groups together.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, group II, claims 7, 39-43, a method for diagnosing prostate cancer, comprising determining the mRNA expression level of a gene encoding PAA3 protein, are examined in the instant application.

OBJECTION

1. Claim 7 is objected to for the use of the language "unaffected" individual. It is not clear that the individual is unaffected by what.

2. Claim 7 is objected to because part of claim 1 is drawn to a non-elected invention, i.e. a method for diagnosing prostate cancer, comprising determining the protein expression level of a gene encoding PAA3 protein.

Claim Rejections - 35 USC § 112 SECOND PARAGRAPH

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 40-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7, 40-43 are indefinite for the use of the language "a gene encoding PAA3" in claim 7.

The specification discloses that PAA3 is the preferred embodiment of a prostate and/or breast cancer "modulating" protein (PCMP and/or BCMP) (p.4, paragraph before last). The specification further discloses that preferably, the prostate/breast cancer sequence is SEQ ID NO:1 (p.8, last paragraph).

It is noted that it is not clear what "modulating" is referred to, because it is a relative term, e.g. modulating could be increasing or decreasing cancer growth, or changing the properties or characteristics of the cancer. It is further noted that a prostate and/or breast cancer modulating protein encompass any protein provided it "modulates" prostate and/or breast cancer.

The definition of PAA3 on page 4 is not limiting, and thus one of ordinary skill in the art would not be reasonably apprised of the metes and bound of the invention.

Further, claims 7, 40-43 are rejected for the use of designation "a gene encoding PAA3" as the sole means of identifying the claimed gene. The use of laboratory

designation only to identify a particular gene renders the claim indefinite because different laboratories may use the same laboratory designations to define completely distinct genes. Amendment of the claims to include physical and/or functional characteristics of "a gene encoding PAA3" which unambiguously define "a gene encoding PAA3" is required.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Claims 7, 39-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 7, 39-43 are drawn to a method for diagnosing prostate cancer, comprising determining the mRNA expression level of a gene encoding PAA3 protein, or SEQ ID NO:1, in a tissue, which is prostate tissue, wherein said determining is carried out using a labeled nucleic acid probe which is immobilized to a solid support.

The specification discloses one isolated PAA3 polynucleotide, SEQ ID NO:1, which is detected to have higher level of expression in prostate cancer as compared to normal tissues and normal prostate tissue, using oligonucleotide microarrays interrogated with cRNAs from prostate cancer tissues or normal tissues including normal prostate tissues. Said cRNAs are generated by *in vitro* transcription (IVT) from cDNA synthesized from mRNAs isolated from the above tissues and then hybridize to oligonucleotide arrays. The specification further discloses that a nucleic acid having the

sequence shown in accession No:AA609723 is used as a probe on the biochips (Example 1 on pages 60- 66, Example 3 on pages 69-70). There is no disclosure whether the sequence shown in accession No:AA609723 is the same as SEQ ID NO:1.

One cannot extrapolate the teaching of the specification to the enablement of the claims because of the following reasons: It is not possible to determine from the information in the specification whether SEQ ID NO:1 could be used as a marker for prostate cancer cells. It is known in the art that the conventional cDNA libraries used for Northerns are made up of a "representative" population of clones from mRNAs isolated from the desired tissues. It is noted that in the instant application, different from the conventional Northerns, cRNAs of the instant application are generated by *in vitro* transcription from cancer or normal tissues and used for hybridization to oligonucleotide arrays before being detected by a nucleic acid probe. It is however well known in the art that *in vitro* transcription for making cRNA by reverse transcription is not always efficient (US 6,271,002B1, column 2, last paragraph, bridging column 3). Further, factors such as the *in vivo* presence of enhancers and/or enhancer binding factors of some gene, that increase the *in vivo* transcription might not be present in *in vitro* transcription, affecting the transcripton efficiency (Lewin, B, ed, 1983, Genes, Jonhn Wiley & Sons, New York, pages 190-191; Mermod, N, 1988, Nautre, 332(6164): 557-61). However, not all genes have enhancers, and therefore, different genes could be differentially effected by the inefficiency of *in vitro* transcription, depending on their structure. In view of the above, it is unpredictable that representative expressed genes in the desired tissues are transcribed into cRNAs by the *in vitro* transcription method in the instant application,

due to the inefficiency and artificial conditions of *in vitro* transcription from cDNAs. The Examiner takes note that mammalian cells contain as many as $1x10^5$ to $3x10^5$ different mRNA molecules, each of which varies in abundance (or frequency) within a given cell (US 6,271,002B1, column 1, lines 60-63). There is however no disclosure of the number of the total original mRNAs represented by cRNAs that are used for hybridization to oligonucleotide arrays. There is no disclosure of whether the disclosed cRNAs are not multiple copies of certain original mRNAs and not representative of certain other original mRNAs. Moreover, there is no disclosure of the number of cRNAs that could be accommodated by the oligonucleotide arrays such that the number of cRNAs are representative of the total original mRNAs. Thus, it is not clear that the genes expressed as cRNAs bound to the oligonucleotide arrays are representative of the original mRNAs. The fact that the sequence of SEQ ID NO:1 is not expressed in one set of cRNAs bound to the oligonucleotide arrays or is expressed in another appears to be an artifact of the analytical system and cannot be extrapolated to a prediction of whether that molecule is expressed in the tissue "represented" in cRNAs bound to the oligonucleotide the arrays.

Further, there is no disclosure whether the sequence shown in accession No:AA609723 which is used as a probe is the same as SEQ ID NO:1 or a gene encoding PAA3. Since there is no correlation between the sequence shown in accession No:AA609723 and SEQ ID NO:1 or a gene encoding PAA3, it is not clear how the sequence shown in accession No:AA609723 could be used for detecting the mRNA expression level of SEQ ID NO:1 or a gene encoding PAA3 in prostate cancer tissues.

Thus the specification does not describe any relationship of a gene encoding PAA3 or SEQ ID NO:1 to the disclosed diseases, or any involvement of the claimed polynucleotides in the etiology of any specific disease.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention as broadly as claimed.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

The claims 7, 40-43 are drawn to a method for diagnosing prostate cancer, comprising determining the mRNA expression level of "a gene encoding PAA3 protein" in a tissue, wherein said determining is carried out using "a nucleic acid probe".

The specification discloses that PAA3 is the preferred embodiment of a prostate and/or breast cancer modulating protein (p.4, paragraph before last). The specification further discloses that preferably, the prostate/breast cancer sequence is SEQ ID NO:1 (p.8, last paragraph).

The specification discloses SEQ ID NO:1, which is detected to have higher level of expression in prostate cancer as compared to normal tissues and normal prostate tissue, using cRNA from prostate cancer tissues and normal tissues including normal prostate tissues hybridized to oligonucleotide microarrays, wherein said cRNAs are

generated by *in vitro* transcription from the above tissues. The specification further discloses that a nucleic acid having the sequence shown in accession No:AA609723 as a probe on the biochips (Example 3 on pages 69-70). There is no disclosure whether the sequence shown in accession No:AA609723 is the same as SEQ ID NO:1.

It is noted that "a gene encoding PAA3 protein" encompasses unrelated polynucleotide sequences, provided they encode proteins that "modulate" prostate and/or breast cancer . Further, a gene encoding PAA3 protein encompasses a genomic DNA encoding PAA3 protein.

In addition, it is noted that "a nucleic acid probe" of claim 40 encompasses any unrelated polynucleotide sequence, which is not necessarily specific for SEQ ID NO:1

The claims, as written, thus encompass a method for diagnosing prostate cancer, comprising determining the mRNA expression level of polynucleotides which vary substantially in length and also in nucleotide composition, using as a probe any polynucleotide sequence.

The instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to

provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed and no identifying characteristic or property of the instant polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

The specification further fails to identify and describe the 5' and 3' regulatory regions and untranslated regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses the gene. The art indicates that the structures of genes with naturally occurring regulatory elements and untranslated regions is empirically determined (Harris et al. J. of The Am Society of Nephrology 6:1125-33, 1995; Ahn et al. Nature Genetics 3(4):283-91, 1993; and Cawthon et al. Genomics 9(3):446-60, 1991). Therefore, the structure of these elements is not conventional in the art and skilled in the art would therefore not recognize from the disclosure that applicant was in possession of the genus of nucleic acid, including genes, comprising SEQ ID NO: 1 or fragments thereof.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific nucleotide sequences and the ability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed. Thus, only a method for diagnosing prostate cancer, comprising determining the mRNA expression level of the polynucleotide sequence of SEQ ID NO:1 in prostate tissue, wherein said determining is carried out using the sequence shown in accession No:AA609723 as a probe, but not the full breadth of the claims meet the written description provisions of 35 USC 112, first paragraph.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

1. If Applicant could overcome the above 112, first paragraph rejection above, claims 7, 43 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting prostate cancer, comprising determining the overexpression of the mRNA level of SEQ ID NO:1 in prostate tissue in a patient, as compared to normal prostate tissue, does not reasonably provide enablement for a method for detecting prostate cancer, comprising determining the mRNA expression of a "gene encoding PAA3", or a fragment thereof, from a first tissue of a first individual , comparing said expression of said gene from a second normal tissue from said first individual or a second unaffected individual, wherein a difference in said expression indicates that the first individual has prostate cancer. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 7, 43 are drawn to a method for detecting prostate cancer, comprising determining the mRNA expression of a "gene encoding PAA3", or a fragment thereof, from a first tissue of a first individual , comparing said expression of said gene from a second normal tissue from said first individual or a second unaffected individual, wherein a difference in said expression indicates that the first individual has prostate cancer.

The specification discloses that PAA3 is the preferred embodiment of a prostate and/or breast cancer modulating protein (p.4, paragraph before last). The specification further discloses that preferably, the prostate/breast cancer sequence is SEQ ID NO:1 (p.8, last paragraph).

The specification also discloses that one isolated PAA3 polynucleotide, SEQ ID NO:1, is detected to have higher level of expression in prostate cancer as compared to normal tissues and normal prostate tissue, using oligonucleotide microarrays interrogated with cRNAs from prostate cancer tissues or normal tissues including normal prostate tissues, wherein said cRNAs are generated by *in vitro* transcription from the above tissues and wherein said cRNAs hybridize to oligonucleotide microarrays. The specification further discloses that a nucleic acid having the sequence shown in accession No:AA609723 is used as a probe on the biochips (Example 3 on pages 69-70).

It is noted that "a gene encoding PAA3 protein" encompasses unrelated polynucleotide sequences, provided they encode proteins that "modulate" prostate and/or breast cancer.

The claims, as written, thus encompass a method for diagnosing prostate cancer, comprising determining the mRNA expression level of unrelated polynucleotides, or of a genomic DNA encoding PAA3 protein.

One cannot extrapolate the teaching of the specification to the scope of the claims because of the following reasons: It is well known in the art that different genes express independently of each other in normal and cancer tissues. Thus it is not clear how detection of the mRNA expression level of unrelated genes would detect prostate cancer.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention as broadly as claimed.

2. If Applicant could overcome the above 112, first paragraph rejection above, claims 7, 43 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting prostate cancer, comprising determining the overexpression of the mRNA level of SEQ ID NO:1 in prostate tissue in a patient, as compared to normal prostate tissue, does not reasonably provide enablement for a method for detecting prostate cancer, comprising determining the mRNA expression of a gene encoding PAA3, or "a fragment thereof", from a first tissue of a first individual , comparing said expression of said gene from a second normal tissue from said first individual or a second unaffected individual, wherein a

difference in said expression indicates that the first individual has prostate cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 7, 43 are drawn to a method for detecting prostate cancer, comprising determining the mRNA expression of a gene encoding PAA3, or "a fragment thereof", from a first tissue of a first individual, comparing said expression of said gene from a second normal tissue from said first individual or a second unaffected individual, wherein a difference in said expression indicates that the first individual has prostate cancer.

The specification also discloses that one isolated PAA3 polynucleotide, SEQ ID NO:1, is detected to have higher level of expression in prostate cancer tissue as compared to normal tissues and normal prostate tissue, using oligonucleotide microarrays interrogated with cRNAs from prostate cancer tissues or normal tissues including normal prostate tissues, wherein said cRNAs are generated by *in vitro* transcription from the above tissues and wherein said cRNAs hybridize to oligonucleotide microarrays. The specification further discloses that a nucleic acid having the sequence shown in accession No:AA609723 is used as a probe on the biochips (Example 3 on pages 69-70).

One cannot extrapolate the teaching of the specification to the scope of the claims because of the following reasons: It is noted a fragment of a gene encoding PAA3 or SEQ ID NO:1 is not necessarily specific for SEQ ID NO:1. Therefore, detection

of the mRNA level of a fragment of a gene encoding PAA3 or SEQ ID NO:1 would be non-specific, wherein the detected unrelated mRNA is not necessarily overexpressed in prostate cancer. For example, detection of fragment of SEQ ID NO:1 would detect the presence of an unrelated polynucleotide present in the testis taught by Oshima A et al, which has 94% similarity with SEQ ID NO:1, from nucleotide 139 to nucleotide 2729, under MPSRCH sequence similarity search (MPSRCH search report, 2003, us-09-847-046-1.rge, pages 6-7) and which is not necessarily overexpressed in prostate cancer.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention as broadly as claimed.

3. If Applicant could overcome the above 112, first paragraph rejection above, claims 7, 39-42 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting prostate cancer, comprising determining the overexpression of the mRNA level of SEQ ID NO:1 in prostate tissue in a patient, as compared to normal prostate tissue, does not reasonably provide enablement for a method for detecting prostate cancer, comprising determining the mRNA expression of a gene encoding PAA3, or a fragment thereof, from "a first tissue" of a first individual , comparing said expression of said gene from "a second normal tissue" from said first individual or a second unaffected individual, wherein a difference in said expression indicates that the first individual has prostate cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 7, 39-42 are drawn to a method for detecting prostate cancer, comprising determining the mRNA expression of a gene encoding PAA3, or SEQ ID NO:1, or a fragment thereof, from a first tissue of a first individual, comparing said expression of said gene from a second normal tissue from said first individual or a second unaffected individual, wherein a difference in said expression indicates that the first individual has prostate cancer.

The specification discloses that one isolated PAA3 polynucleotide, SEQ ID NO:1, is detected to have higher level of expression in prostate cancer tissue as compared to normal tissues and normal prostate tissue, using oligonucleotide microarrays interrogated with cRNAs from prostate cancer tissues or normal tissues including normal prostate tissues, wherein said cRNAs are generated by *in vitro* transcription from the above tissues and wherein said cRNAs hybridize to oligonucleotide microarrays. The specification further discloses that a nucleic acid having the sequence shown in accession No:AA609723 is used as a probe on the biochips (Example 3 on pages 69-70).

One cannot extrapolate the teaching of the specification to the scope of the claims because of the following reasons: Although SEQ ID NO:1 is overexpressed in prostate cancer tissue, it is unpredictable that it is overexpressed in any other tissue in a prostate cancer patient, because it is well known in the art that expression of a gene in different tissue is independent of each other. Further, one cannot predict that metastatic prostate cancer cells which may locate in tissues other than prostate cancer tissue, would overexpress SEQ ID NO:1, because expression of a sequence could be lost

during the progression toward metastasis. For example, Kibel, AS et al, 2000, J urol, 164(1): 192-6 teach that gene expression in the chromosomal region 12p12-13 is different in primary and metastatic cells, and that inactivation in the chromosome region 12p12-13 occurs prior to metastasis. Ren, C et al, 1998, Cancer Res, 58(6): 1285-90, teach a loss of expression of lysyl oxidase mRNA during progression to metastasis. Gingrich, JR et al, 1996, Cancer res, 56(18): 4096-4102 teach a loss of normal E-cadherin expression as primary tumors become less differentiated and metastasize. Thus, it is unpredictable that SEQ ID NO:1 is overexpressed in any other tissue in a prostate cancer patient.

Further, not any normal tissue other than normal prostate tissue could be used as a control, because difference in the expression of SEQ ID NO:1 in prostate cancer tissue as compared to any normal tissue other than normal prostate tissue would only indicate that SEQ ID NO:1 is prostate specific, and not necessarily overexpressed.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention as broadly as claimed.

4. If Applicant could overcome the above 112, first paragraph rejection above, claims 7, 39-43 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting prostate cancer, comprising determining the overexpression of the mRNA level of SEQ ID NO:1 in prostate tissue in a patient, as compared to normal prostate tissue, does not reasonably provide enablement for a method for detecting prostate cancer, comprising determining the mRNA expression of a gene encoding PAA3, or a fragment thereof, from a first

tissue of a first individual , comparing said expression of said gene from a second normal tissue from said first individual or a second unaffected individual, wherein "a difference" in said expression indicates that the first individual has prostate cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 7, 39-43 are drawn to a method for detecting prostate cancer, comprising determining the mRNA expression of a gene encoding PAA3, or SEQ ID NO:1, or a fragment thereof, from a first tissue of a first individual, comparing said expression of said gene from a second normal tissue from said first individual or a second unaffected individual, wherein "a difference" in said expression indicates that the first individual has prostate cancer.

The specification discloses that one isolated PAA3 polynucleotide, SEQ ID NO:1, is detected to have higher level of expression in prostate cancer tissue as compared to normal tissues and normal prostate tissue, using oligonucleotide microarrays interrogated with cRNAs from prostate cancer tissues or normal tissues including normal prostate tissues, wherein said cRNAs are generated by *in vitro* transcription from the above tissues and wherein said cRNAs hybridize to oligonucleotide microarrays. The specification further discloses that a nucleic acid having the sequence shown in accession No:AA609723 is used as a probe on the biochips (Example 3 on pages 69-70).

One cannot extrapolate the teaching of the specification to the scope of the claims because of the following reasons: It is noted that a "difference" in the expression of a gene encoding PAA3 or SEQ ID NO:1 means either an increase or a decrease in the expression of said gene, which is opposite from each other. In view of a single disclosure in the specification that SEQ ID NO:1 is overexpressed in prostate cancer tissue as compared to normal prostate tissue, it is unpredictable that a gene encoding PAA3 or SEQ ID NO:1 would decrease in expression in prostate cancer, because the level of expression of a gene in cancer tissue is not predictable.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention as broadly as claimed.

5. If Applicant could overcome the above 112, first paragraph rejection above, claims 40-42 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting prostate cancer, comprising determining the overexpression of the mRNA level of SEQ ID NO:1 in prostate tissue in a patient, as compared to normal prostate tissue, wherein said determining is carried out using the sequence shown in accession No:AA609723 as a probe, does not reasonably provide enablement for a method for detecting prostate cancer, comprising determining the mRNA expression of SEQ ID NO:1, from a first tissue of a first individual , comparing said expression of said gene from a second normal tissue from said first individual or a second unaffected individual, wherein said determining is carried out using "a nucleic acid probe", and wherein a difference in said expression indicates that the first individual has prostate cancer. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 40-42 are drawn to a method for detecting prostate cancer, comprising a) determining the mRNA expression of SEQ ID NO:1, from a first tissue of a first individual, using a "nucleic acid probe", b) comparing said expression of said gene from a second normal tissue from said first individual or a second unaffected individual, wherein a difference in said expression indicates that the first individual has prostate cancer.

The specification discloses that one isolated PAA3 polynucleotide, SEQ ID NO:1, is detected to have higher level of expression in prostate cancer tissue as compared to normal tissues and normal prostate tissue, using oligonucleotide microarrays interrogated with cRNAs from prostate cancer tissues or normal tissues including normal prostate tissues, wherein said cRNAs are generated by *in vitro* transcription from the above tissues and wherein said cRNAs hybridize to oligonucleotide microarrays. The specification further discloses that a nucleic acid having the sequence shown in accession No:AA609723 is used as a probe on the biochips (Example 3 on pages 69-70).

One cannot extrapolate the teaching of the specification to the scope of the claims because of the following reasons: It is noted that "a nucleic acid probe" encompasses any unrelated polynucleotide sequence, which is not necessarily specific

for SEQ ID NO:1. Thus it is not clear how any nucleic acid probe could be used for the detection of the expression of SEQ ID NO:1.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention as broadly as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 7, 39-43 are rejected under 35 U.S.C. 102(e) as being anticipated by PCT/US 01/05171.

Claims 7, 39- 43 are drawn to a method for diagnosing prostate cancer, comprising a) determining the mRNA expression of a gene encoding PAA3 or SEQ ID

NO:1, from a first tissue of a first individual, using a "nucleic acid probe", b) comparing said expression of said gene from a second normal tissue from said first individual or a second unaffected individual, wherein a difference in said expression indicates that the first individual has prostate cancer. The first tissue is prostate tissue. Said determining is carried out using a labeled nucleic acid probe or a nucleic acid probe which is immobilized to a solid support.

remain PCT/US 01/05171 teaches a method for assessing whether a patient is afflicted with prostate cancer, comprising comparing the level of expression of a marker in tables 1-9 in a patient sample, which is a prostate tissue, with the normal level of expression of said marker in a control prostate cancer sample, wherein a significant difference between the level of expression of the patient sample and the normal level is an indication that the patient is afflicted with prostate cancer (claims 18, 27). PCT/US 01/05171 teaches the use of a probe which is labeled for detection of prostate cancer cells (p.10, last paragraph, bridging p.11, p. 18, last paragraph, and claim 47) or a probe which is fixed to a substrate (p.19, first paragraph). PCT/US 01/05171 further teaches human prostate expression marker cDNA 21958 from Library cMhqal (table 8, and page 96, second paragraph). Under MPSRCH sequence similarity search, SEQ ID NO:1 is 97% similar to marker cDNA 21958 from nucleotide 1664 to nucleotide 4363 (MPSRCH search report, 2003, us-09-847-046-1.rng, pages 6-7). Considering the extensive homology between SEQ ID NO:1 and the marker cDNA 21958, and no disclosure of specific probe in the specification and the claims, one would expect that the method taught by PCT/US 01/05171 would also detect the claimed sequence of SEQ ID NO:1.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

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April 18, 2003

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